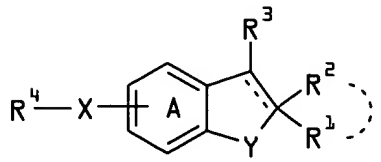
Version with Markings to Show Changes Made

In the Claims

11. (THRICE AMENDED) A compound of **[Claim 1,]** **the formula:**



wherein R^1 and R^2 **are** each **[is]** a C_{1-6} alkyl or R^1 and R^2 form, taken together with the adjacent carbon atom, a piperidine optionally substituted by 1 to 3 substituents selected from the group consisting of C_{1-6} alkyl, C_{6-14} aryl and C_{7-16} aralkyl;

R^3 is a phenyl optionally substituted by 1 to 3 substituents selected from the group consisting of halogen atoms, C_{1-6} alkyl, C_{1-6} alkoxy, amino, mono-C_{1-6} alkylamino and di-C_{1-6} alkylamino;

R^4 is

(i) C_{1-6} alkyl substituted by a phenyl or pyridyl, each of which is optionally substituted by 1 to 3 substituents selected from the group consisting of halogen atoms, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino and carboxy, or

(ii) an acyl of the formula: -(C=O)-$R^{5'}$ wherein $R^{5'}$ is a phenyl or phenyl-C_{1-6} alkyl, each of which is optionally substituted by 1 to 3 substituents selected from the group consisting of halogen atoms, C_{1-6} alkyl, C_{1-6} alkoxy, hydroxy, amino, mono-C_{1-6} alkylamino, di-C_{1-6} alkylamino and carboxy;

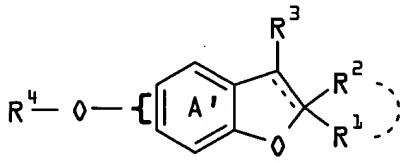
X is an oxygen atom;

Y is an oxygen atom; and

ring A is a benzene ring which is optionally further substituted by 1 to 3 substituents selected from the group consisting of halogen atoms, halogenated or unhalogenated C_{1-6} alkyl, halogenated or unhalogenated C_{1-6} alkoxy, amino, mono-C_{1-6} alkylamino and di-C_{1-6} alkylamino,

and salts thereof.

12. (THRICE AMENDED) A compound **[of Claim 1 which is a compound]** of the formula:



wherein R^1 and R^2 **are** each **[is]** C_{1-6} alkyl or R^1 and R^2 form, taken together with the adjacent carbon atom, a piperidine substituted by a C_{1-6} alkyl or a C_{7-16} aralkyl;

R^3 is a phenyl optionally substituted by 1 to 3 substituents selected from the group consisting of (1) C_{1-6} alkyl, (2) di-C_{1-6} alkylamino and (3) 6-membered saturated cyclic amino optionally substituted by a C_{1-6} alkyl,

R^4 is

(i)a phenyl optionally substituted by 1 to 3 substituents selected from the group consisting of nitro and C_{1-6} alkyl-carboxamido,

(ii) a C_{1-6} alkyl or C_{2-6} alkenyl group substituted by 1 to 3 of phenyl, quinolyl or pyridyl, each of which is optionally substituted by 1 to 3 substituents selected from the group consisting of C_{1-6} alkoxy, C_{1-6} alkylthio, C_{1-6} alkoxy-carbonyl, C_{1-6} alkylsulfonyl and C_{1-6} alkylsulfinyl, which C_{1-6} alkyl or C_{2-6} alkenyl group is optionally further substituted by a phenyl, carboxy or C_{1-6} alkoxy-carbonyl, or

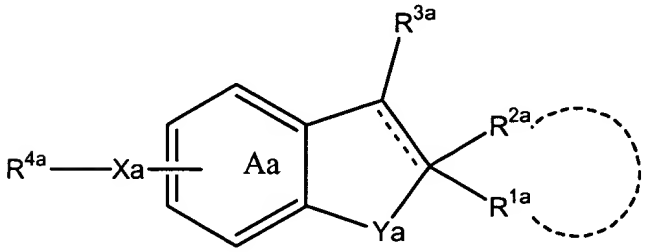
(iii) an acyl of the formula: $-(C=O)-R^{5''}$

wherein $R^{5''}$ is phenyl substituted by a C_{1-6} alkoxy; and

ring A' is a benzene ring which is optionally further substituted by 1 to 3 C_{1-6} alkyl, **and salts thereof**.

13. (THRICE AMENDED) **[A compound of Claim 1 which is]** 3-(4-isopropylphenyl)-2,4,6,7-tetramethylbenzofuran-5-yl 4-methoxybenzoate, 3-(4-isopropylphenyl)-5-(4-methoxybenzyloxy)-2,4,6,7-tetramethylbenzofuran, 3-(4-isopropylphenyl)-5-(4-methoxybenzyloxy)-1',4,6,7-tetramethylspiro(benzofuran-2(3H), 4'-piperidine), or a salt thereof.

22. (FIVE TIMES AMENDED) A method for suppressing β-amyloid toxicity in a mammal, which comprises administering to said mammal an effective amount of a compound of the formula:



wherein R^{1a} and R^{2a} each represents a hydrogen atom or a hydrocarbon group which is optionally substituted, or R^{1a} and R^{2a} form, taken together with the adjacent carbon atom, a 3- to 8-membered carbo or heterocyclic unsubstituted or substituted ring;

R^{3a} represents a hydrogen atom or an unsubstituted or substituted **[aromatic]** **phenyl** group;

R^{4a} represents an **[unsubstituted or substituted aromatic group, an]** unsubstituted or substituted aliphatic hydrocarbon group **[or an acyl]**;

Xa represents an oxygen atom;

Ya represents an oxygen atom;

---- represents a single bond or a double bond;

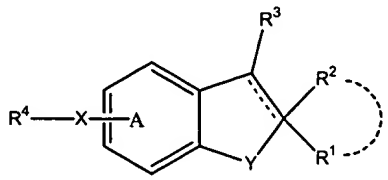
ring Aa represents a benzene ring which is optionally further substituted apart from (i) the group of the formula: -Xa-R^{4a} wherein each symbol is as defined above, and (ii) an unsubstituted or substituted amino,

[provided that when ---- is a single bond, R^{4a} is not an acyl,]

or a **[pharmaceutically acceptable]** salt thereof

[with a pharmaceutically acceptable excipient, carrier or diluent].

25. (THRICE AMENDED) A method for suppressing β-amyloid toxicity in a mammal, which comprises administering to said mammal an effective amount of a compound of the formula:



wherein R^1 and R^2 each represent an acyclic hydrocarbon group**[,]** **or** a cycloalkyl group**[, or R^1 and R^2 form, taken together with the adjacent carbon atom, a 3- to 8-membered carbo or heterocyclic unsubstituted or substituted ring]**;

R^3 represents an unsubstituted or substituted **[aromatic]** **phenyl** group;

R^4 represents **[(1) an unsubstituted or substituted aromatic group, (2)]** an aliphatic hydrocarbon group substituted by an unsubstituted or substituted aromatic group, which hydrocarbon group is optionally further substituted **[or (3) an acyl]**;

X and Y each represent an oxygen atom;

------- represents a single bond or a double bond;

and Ring A represents a benzene which is optionally further substituted apart from the group of the formula: -X-R^4 wherein each symbol is as defined above,

[provided that when ------- is a single bond, R^4 is not an acyl,]

or a salt thereof

[with a pharmaceutically acceptable excipient, carrier or diluent].

REMARKS

I. Amendments

By this amendment, claims 11-13, 22 and 25 have been amended.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "Version with Markings to Show Changes Made".

No amendment of inventorship is necessitated by this amendment.

II. Second Request For Examiner's Acknowledgement of Previously Submitted Information Disclosure Statement

Applicants filed an Information Disclosure Statement of December 2, 1999. In paper no. 8, the 1449 was attached, but several of the references were lined through. The Examiner indicated that not all references were initialed because not all references had not been received. On February 2, 2001, Applicants submitted copies of these references to the Examiner. However, these references were not acknowledged by the Examiner in a subsequent Office Action summary. Applicants request that the Examiner inform them if the copies of the references mailed February 2, 2001 were not received. If they were received, Applicants respectfully request that the Examiner provide them with an initialed form 1449.

Applicants made this request in the response dated February 7, 2002, which was unacknowledged in the Office Action dated June 13, 2002. Applicants respectfully request the Examiner's attention to this matter.

III. Discussion of the Rejection of Claims 1-3, 5, 8-15 and 22 under 35 U.S.C. Sec. 112, First Paragraph

Claims 1-3, 5, 8-15 and 22 have been rejected under 35 U.S.C. Sec. 112, first paragraph. The Examiner stated that the specification does not reasonably provide enablement for R^4 being other than moieties indicated on pages 103-105 and R^3 being other than phenyl substituted with a

dimethyl group. Applicants will respond to each of the Examiner's objections in separate sections below.

A. Enablement for Y

Applicants note that in their previous amendment, Y had been limited to oxygen in the claims. However, in Section one of the Office Action, the Examiner has made several references to Y which do not seem to acknowledge the status of the claims as currently limited with respect to Y. Therefore Applicants respectfully request the Examiner's acknowledgement of the enablement of Y.

B. Enablement for R^3

The Examiner's argument appears to be directed to the fact that the cell protecting activity of only 7 compounds was actually tested, as shown on page 109 of the specification, and that Applicants' invention as set forth in the present claims is of greater breadth than the 7 compounds tested. Applicants wish to draw the Examiner's attention to the fact that independent claim 1 is a composition of matter claim. As such the enablement for the claim resides in the synthesis of representative compounds, not subsequent activity testing. Applicants provide the argument made in their previous amendment again here; that several compounds ***were*** synthesized wherein R^3 represents various species; and that accordingly the compounds set forth in claim 1 are fully enabled.

As previously indicated, Applicants ***have*** synthesized compounds representing a broader range of substitutents than just the "phenyl substituted with a dimethyl group" which the Examiner has indicated is enabled. In fact, the Examiner's characterization of "phenyl substituted with a dimethyl group " as enabled is not even correct. With reference to pages 103-105 of the specification and that substituent c represents R^3 of claim 1, Applicants note that they have synthesized several compounds wherein c (R^3) is a phenyl group having an isopropyl group substituted in the *para* position. Applicants surmise that the Examiner may have intended to indicate that phenyl groups substituted with an isopropyl group were enabled, instead of a dimethyl-substituted phenyl group. Applicants respectfully request that the Examiner carefully reconsider her viewpoint.

Applicants have synthesized compounds with R^3 other than isopropyl, which they believe provide ample support for the enablement of the current definition of R^3 in claim 1. Specificially, in Examples 3 and 31, c = H; in Example 28, c is unsubstituted phenyl and in Examples 2 and 6-8, substituents of phenyl other than an isopropyl group are exemplified. Therefore, Applicants submit that their current definition of R^3 as "an unsubstituted or substituted aromatic group" in claim 1 is fully enabled by the specification. To assist the Examiner's analysis of this matter, Applicants have provided an attached Appendix A, wherein pages 103-105 have been marked to indicate the synthesized compounds which fully enable Applicants' definition of R^3.

Furthermore, a detailed description of appropriate substituents for R^3 is found on page 33, line 21 – page 36, line 11 of the specification. Production methods for compounds representative of the invention as set forth in claim 1 are described in detail on page 49, line 31 – page 60, line 31. As indicated above, several specific synthetic examples are provided, wherein R^3 is represented by hydrogen or various substituted or unsubstituted phenyl groups. Therefore, the specification provides adequate information for one skilled in the art to make compounds containing aromatic groups other than optionally phenyl rings or hydrogen for R^3.

Claims 2, 3, 5 and 8-15 are also composition of matter claims, dependent upon claim 1. Applicants submit that these more specific dependent claims are also enabled for the reason provided above.

Most particularly, Applicants note that in claims 11 and 12, R^3 is already limited to optionally substituted phenyl groups, so Applicants insist that these claims are commensurate in scope with the teachings of the specification.

Furthermore, the present claim 13 lists three specific compounds, each having a 4-isopropylphenyl group for R^3, which Applicants also insist is fully enabled by the specification.

By this amendment, claims 11-13 have been made independent, to ensure their separate consideration by the Examiner.

Claim 14 is a method of making the compounds set forth in claim 1, and claim 15 is a composition of compounds of claim 1. Applicants submit that these more specific dependent claims also enabled for the reason provided above.

Claim 22 is an independent claim directed to a method for suppressing β-amyloid toxicity, wherein R^{3a} is a hydrogen atom or an optionally substituted phenyl group, as amended. Applicants submit that their definition of R^{3a} as amended is fully enabled by the specification.

C. Enablement for R^4

As the Applicants have previously indicated, R^4, as set forth in claim 1, is fully supported by the specification. To assist the Examiner's analysis of this matter, Applicants have provided an attached Appendix A, wherein pages 103-105 have been marked to indicate the synthesized compounds which fully enable Applicants' definition of R^4. Applicants will explain in detail below how each of the three types of groups indicated in claim 1 as possibilities for R^4 is supported by an actual synthetic example.

On pages 103-105, R^4 is signified by substituents d, e, f and g in the generic structure at the top of each page. Note that X is defined as oxygen in claim 1.

Therefore support for the first type of substituent "an unsubstituted or substituted aromatic group" for R^4 in claim 1 may be found in Examples 20 and 21 on page 104, substituent e, wherein examples of R^4 as a substituted aromatic group are provided.

Support for the second type of substituent for R^4 in claim 1 "an aliphatic hydrocarbon group substituted by an unsubstituted or substituted aromatic group, which hydrocarbon group is optionally further substituted" may be found in Examples 15, 23 and 24, on page 104 substituent e, wherein examples of R^4 as an aliphatic hydrocarbon group substituted by an unsubstituted or substituted aromatic group are provided.

Support for the third type of substituent for R^4 in claim 1 "an acyl" can be found in Examples 26 and 28, on page 104 substituent e, wherein acyl groups are listed.

Therefore, Applicants believe that they have adequately demonstrated that the current definition of R^4 in claim 1 is fully enabled.

Claims 2, 3, 5 and 8-15 are also composition of matter claims, dependent upon claim 1. Applicants submit that these more specific dependent claims are also enabled for the reason provided above.

Most particularly, Applicants note that in claims 11 and 12, R^4 is even more limited than the definition in claim 1, so Applicants insist that these claims are commensurate in scope with the teachings of the specification.

Furthermore, the present claim 13 lists three specific compounds, which Applicants also insist are fully enabled by the specification.

By this amendment, claims 11-13 have been made independent, to ensure their separate consideration by the Examiner.

Claim 14 is a method of making the compounds set forth in claim 1, and claim 15 is a composition of compounds of claim 1. Applicants submit that these more specific dependent claims also enabled for the reason provided above.

Claim 22 is an independent claim directed to a method for suppressing β-amyloid toxicity, wherein R^{4a} represents an unsubstituted or substituted aliphatic hydrocarbon group, as amended. Applicants submit that their definition of R^{4a} as amended is fully enabled by the specification.

For the detailed reasons provided above, Applicants believe that their invention as set forth in the present claims as amended is fully enabled by the specification. Therefore, Applicants respectfully request withdrawal of the Sec. 112, first paragraph rejection.

IV. Discussion of the Rejection of Claims 26-28 under 35 U.S.C. 112, First Paragraph

Claims 26 and 28 have been rejected under 35 U.S.C. Sec. 112, first paragraph for allegedly lacking enablement. The Examiner stated that the specification does not reasonably provide enablement for R^{4a} being other than moieties indicated on pages 103-105 and R^{3a} being other than phenyl substituted with a dimethyl group. Applicants do not understand the logical reasoning for this rejection, as explained below.

In Section 2 of the Office Action, the Examiner has made references to diseases such as Parkinson's and Huntington's chorea; as well as made references to Y as sulfur. Applicants do not understand why such comments have been included, as claims 26 and 28 are limited to a single disease (Alzheimer's) by virtue of the previous amendment; and Y is already limited to only oxygen, by virtue of the previous amendment. Moreover, as stated above "R^{3a} as phenyl substituted with a dimethyl group" is an incorrect characterization of the Applicants' invention. Furthermore, claim 26 depends upon claim 25 while claim 28 depends upon claim 22. If the Examiner actually meant to reject the claims on the basis of allegedly unenabled definitions for R^3 and R^4, Applicants assume that the base claims 22 and 25 should have been included in this rejection. Conversely, if the nature of the rejection was due to "treating all of the various diseases" as the Examiner stated on page 4 of the Office Action, the rejection has been overcome by the previous amendment.

In light of all of these inconsistencies, Applicants respectfully request the Examiner's attentive re-consideration and withdrawal of the Sec. 112, first paragraph rejection.

V. Discussion of Rejection of Claim 25 under 35 U.S.C. Sec. 112, First Paragraph

Claim 25 has been rejected under 35 U.S.C. Sec. 112, first paragraph as allegedly unenabled for R^1 and R^2 when the substitutents are combined to form a ring.

By this amendment, claim 25 has been limited to R^1 and R^2 of acyclic hydrocarbon groups or cycloalkyl groups. Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 112, first paragraph rejection.

VI. Conclusion

Reconsideration of the claims as amended and allowance is requested.

Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, she is respectfully requested to call Applicants' attorney at (847) 383-3391.

Respectfully submitted,

Dated: September 24, 2002

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